REMARKS

This application pertains to a novel abuse-proofed dosage form.

Claims 1, 2, 4, 7, 8, 27- 29, 31, 41 and 42 are pending.

Claim 42 is amended to limit the amount of component (C) of claim 1 to at least 30% by weight. Support for this limitation is found in Example 5, where 90 mg. of polyethylene oxide is included in a dosage form having a total weight of 300 mg.

Claims 1, 2, 4, 6-8, 29, 31, 41 and 42 stand provisionally rejected for obviousness type double patenting over claims 1-4, 7-11, 25-27 and 30 of copending application No. 10/567,594. This provisional rejection is obviated by the accompanying Terminal Disclaimer. This Terminal Disclaimer is identical to the one submitted on February 17, 2009, except that the typographical error in the serial number "10/5***5***7,594" has been corrected to --10/567,594--.

Claim 1 stands objected to because it ended in two periods. The claim has now been amended to cancel one of said periods, thereby obviating the objection. The objection to claim 1 should therefore now be withdrawn.

Claims 1, 2, 4, 7, 8, 27-29, 31, 41 and 42 stand rejected under 35 U.S.C. 103(a) as obvious over Oshlack et al (US 2003/0064099/A1).

Applicants' claims require that the breaking strength of Applicants' dosage form be at least 500 N. The Oshlack reference clearly teaches away from such a breaking strength in that it is an essential character of Oshlack's oral dosage form that it be chewable. See Oshlack's paragraph [0055]. Such chewing is essential in order for Oshlack's aversive agent to be released. If Oshlack's dosage form was too hard to be chewed, the aversive agent would not be released and Oshlack's mechanism for discouraging tampering with the dosage form would not be realized.

As can be seen from the accompanying publication Proeschel, J Dent. Res 81 (7):464-468, 2002, the mean human chewing force is about 200 N, which means that the breaking strength of Oshlack's dosage form must be no more than about 200 N; otherwise it could not be chewed and the aversive agent could not be released.

Moreover, Applicants claims require that the active ingredient be present in a controlled release matrix of polyethylene oxide having a molecular weight of 1-15 g/mol.

Oshlack et al. mentions polyalkylene oxide having a molecular weight of at least 0.5 million. Nevertheless, the only disclosure of these polymers is

exclusively concerned with osmotic dosage forms (Oshlack et al., [0148]-[0159]), which, however, are not thermoformed.

In another context, Oshlack et al. mentions methods for the preparation of matrix formulations which methods may be regarded as thermoforming, such as melt-extrusion (Oshlack et al., [0111]). These matrix materials according to Oshlack at al., however, do not encompass polyalkylene oxides (Oshlack et al., [0097]).

Furthermore, in the dosage form according to claim 1 of the present application, the active ingredient is present in a controlled-release matrix of component (C). The active ingredient is embedded in the high molecular weight polyalkylene oxide that in turn serves as a retardant agent (specification, page 35, lines 13-19).

In contrast thereto, the release profile of the osmotic dosage forms according to Oshlack at al. does not rely on a controlled-release matrix, but on the expansion of the waterswellable high molecular polyalkylene oxides in the push layer, which does not contain the drug.

In other words, in the dosage forms according to the subject invention the high molecular weight polyalkylene oxide serves as a controlled-release matrix thereby retarding the release profile of the drug. In contrast thereto, in the osmotic dosage forms according to and Oshlack et al. *a* semi-permeable membrane

hinders the drug from being released and the swelling of the high molecular weight polyalkylene oxide rather causes the drug to leave the dosage form by pushing it through an orifice in the semi-permeable membrane.

Therefore, the effect of the high molecular weight polyalkylene oxide in the matrix dosage forms of the present invention and in the osmotic dosage forms of the Oshlack reference are directly opposite to each other.

Further, Applicants' claims are limited to the use of polyethylene oxide having a molecular weight of 1-15 million, according to rheological measurements. Oshlack mentions the use of polyethylene oxide as a gelling agent, but does not teach or suggest anything about the use of polyethylene oxide having a molecular weight of 1-15 million. As can be seen from the attached product description sheets the chemical supplier SIGMA-ALDRICH® commercializes polyethylene oxides having molecular weights of 10,000 g/mol and 100,000 g/mol, respectively, i.e. molecular weights which are 10 times and 100 times lower than the lower limit according to instant claim 1. Accordingly, Oshlack's disclosure of the use of polyethylene oxide as a gelling agent does not teach or suggest anything about the inclusion of polyethylene oxide in the 1-15 million molecular weight range as a hardening agent.

Further yet, Applicants' dosage forms require that the polyalkylene oxide be present in an amount sufficient to result in a breaking strength of at least

500 N. As shown by the accompanying Rule 132 declaration, lesser amounts of polyethylene oxide did not achieve Applicants' breaking strength.

There is nothing in the reference that would teach or suggest anything about even the possibility of achieving such a breaking strength under any circumstances, let alone any hint that this could be achieved by including a sufficient amount of polyalkylene oxide and sintering.

Still further, Oshlack et al. is not a broad general disclosure containing a vast number of features that a skilled person would readily combine with one another, but a disclosure of distinct dosage forms having distinct properties based on distinct excipients and distinct processes of manufacture.

Oshlack et al. contains various sections dealing with different concepts of pharmaceutical technology by which to realize different dosage forms, each section containing a separate heading, e.g.:

- coated beads [0084]
- matrix formulation [0096]
- osmotic dosage forms [0148]
- transdermal delivery systems [0160]
- suppositories [0168].

A skilled person is fully aware that each section deals with another type of dosage form. A skilled person would not follow the Examiner's approach to arbitrarily pick individual features that are only disclosed in connection with a particular type of dosage form and combining them with other features disclosed in connection with other particular types of dosage forms.

The dosage forms according to the present invention can be regarded neither as coated beads, nor as osmotic dosage forms, nor as transdermal delivery systems nor as suppositories.

Rather, the dosage forms according to the present invention can be regarded as matrix formulations where the polyalkylene oxide having a molecular weight of 1-15 million g/mol forms a matrix in which the active ingredient is embedded.

According to Oshlack et al., however, polyethylene oxide is not among the matrix materials disclosed therein.

In this regard, Oshlack et al. merely discloses:

> **[0097]** A non-limiting list of suitable sustained-release materials which may be included in a sustained-release matrix according to the invention includes hydrophilic and/or hydrophobic materials, such as gums, cellulose ethers, acrylic resins, protein derived materials, waxes, shellac, and oils such as hydrogenated castor oil and hydrogenated vegetable oil. However, any pharmaceutically acceptable hydrophobic or hydrophilic sustained-release material which is capable of imparting sustained-release of the opioid analgesic may be used in accordance with the present invention. Preferred sustained-release polymers include alkylcelluloses such as ethylcellulose, acrylic and methacrylic acid polymers and copolymers; and cellulose ethers, especially hydroxyalkylcelluloses (especially hydroxypropylmethylcellulose) and carboxyalkylcelluloses. Preferred acrylic and methacrylic acid polymers and copolymers include methyl methacrylate, methyl methacrylate copolymers, ethoxyethyl methacrylates, ethyl acrylate, trimethyl ammonioethyl methacrylate, cyanoethyl methacrylate, aminoalkyl methacrylate copolymer, poly(acrylic acid), poly(methacrylic acid), methacrylic acid alkylamine copolymer, poly(methylmethacrylate), poly(methacrylicacid) (anhydride), polymethacrylate, polyacrylamide, poly(methacrylic acid anhydride), and glycidyl methacrylate copolymers. Certain preferred embodiments utilize mixtures of any of the foregoing sustained-release materials in the matrix of the invention.

In fact, the entire section dealing with matrix formulations according to Oshlack et al. is completely silent on polyalkylene oxide having a molecular weight of 1-15 million g/mol.

Analogously, as the section dealing with matrix formulations according to Oshlack et al. is the only section mentioning hot-melt extrusion technique - which the Examiner "considers" as a sintering method (Oshlack et al., [0111]-[0129]), the feature combination {polyalkylene oxide + hot melt-extrusion/sintering}, let alone the feature combination {polyalkylene oxide having a molecular weight of

1-15 million g/mol + hot-melt extrusion/sintering} cannot be derived from Oshlack et al.

Those skilled in the art understand that hot-melt extrusion and sintering are two entirely different concepts, and that the morphology of a dosage form prepared by hot-melt extrusion differs from the morphology of a sintered dosage form according to the present invention. The Examiner's contention that "The melt-extrusion technique of Oshlack et al encompasses the sintering technique of the instant claims..." is totally without merit. Those skilled in the art are well aware of melt-extrusion, and no person skilled in the art would ever argue that melt-extrusion encompasses "sintering". These are two different concepts, and neither encompasses the other.

The only disclosure of Oshlack et al. concerning polyethylene oxide having a molecular weight within the range of instant claim 1 of the present application is in connection with delivery or push layers of osmotic dosage forms (Oshlack et al., [0150]-[0151]).

Said delivery or push layers of osmotic dosage forms, however, do not contain the drug. Instead, in osmotic dosage forms the drug is contained in a drug layer that is separate from said delivery or push layer.

Accordingly, in the osmotic dosage forms according to Oshlack et al. the drug is not present in a controlled release matrix of the polyethylene oxide having a molecular weight of 1-15 million g/mol.

In addition, there is no hint in Oshlack et al. of any osmotic dosage forms prepared by hot melt-extrusion. Thus, also when starting from this section of Oshlack et al., the combination {polyalkylene oxide + hot melt-extrusion }, let alone the feature combination {polyalkylene oxide having a molecular weight of 1-15 million g/mol + hot-melt extrusion } cannot be derived, let alone that the opioid is present in a matrix of the polyalkylene oxide or that the dosage form is sintered.

In sum, various arbitrary selections from distinct sections of Oshlack et al. are relied upon by the Examiner in her attempt to arrive at the feature combination of instant claim 1, i.e. that the active ingredient is present in a controlled release matrix of polyethylene oxide having a molecular weight of 1-15 million g/mol.

Such arbitrary selections are contrary to the general technical understanding that would be reached by those skilled in the art from a reading of Oshlack et al. and merely represent an artificial approach based on an attempt at hindsight reconstruction.

Applicants' claims cannot therefore be seen as obvious over the disclosure of Oshlack, and the rejection of claims 1, 2, 4, 7, 8, 27-29, 31, 41 and 42 under 35 U.S.C. 103(a) as obvious over Oshlack et al (US 2003/0064099/A1) should now be withdrawn.

In view of the present amendments and remarks it is believed that claims 1, 2, 4, 7, 8, 27-29, 31, 41 and 42 are now in condition for allowance. Reconsideration of said claims by the Examiner is respectfully requested and the allowance thereof is courteously solicited.

CONDITIONAL PETITION FOR EXTENSION OF TIME

If any extension of time for this response is required, Applicants request that this be considered a petition therefor. Please charge the required petition fee to Deposit Account No. 14-1263.

ADDITIONAL FEE

Please charge any insufficiency of fee or credit any excess to Deposit Account No. 14-1263.

Respectfully submitted,
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